# Generation of safe and therapeutically effective human induced hepatocyte-like cells

## Grant Award Details

Generation of safe and therapeutically effective human induced hepatocyte-like cells

**Grant Type:** Early Translational III

**Grant Number:** TR3-05542

**Project Objective:** Goal = develop a source of autologous liver cells for patients who otherwise would require a liver transplant.
PI already has the ability to generate induced hepatocytes from human embryonic cells and seeks to identify methods to generate same from human adult cells using transient gene transfer methods and possibly small molecules. POC for iHep cell function will be tested in small and large animal models of liver failure.

**Investigator:**

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| **Name:** | Holger Willenbring |
| **Institution:** | University of California, San Francisco |
| **Type:** | PI |

**Disease Focus:** Liver Disease

**Collaborative Funder:** China

**Human Stem Cell Use:** Directly Reprogrammed Cell

**Award Value:** $1,544,170

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 1

**View Report**

**Reporting Period:** Year 2

**View Report**

**Reporting Period:** Year 3

**View Report**

**Reporting Period:** Year 4

**View Report**

## Grant Application Details

**Application Title:** Generation of safe and therapeutically effective human induced hepatocyte-like cells

**Public Abstract:** Although the liver can regenerate itself, chronic or overwhelming damage can cause life-threatening liver failure. Currently, the only therapy for liver failure is liver transplantation. Because the supply of cadaveric livers or liver tissue from living donors far exceeds the demand, physicians and researchers seek to develop new therapies to save the lives of patients with liver failure. One promising strategy is transplantation of hepatocytes, the cells of the liver that provide most of its functions and that are defective in liver failure. To make hepatocyte transplantation available to all patients who could benefit, a cell source other than scarce donor livers has to be established. In contrast to hepatocytes, skin cells can be readily obtained and expanded in culture. Therefore, the recent discovery that skin cells can be converted into hepatocytes by transfer of a few genes suggests a promising new source of hepatocytes. To develop transplantation of such cells as a therapy for liver failure, we aim to identify which readily available human cell type—skin, blood or fat cells—can be most efficiently converted into hepatocytes using methods of temporary gene transfer. Importantly, the therapeutic efficacy and safety of these induced hepatocytes will be rigorously tested in animal models of human liver failure. If successful, our project will establish the feasibility of therapy of liver failure with cells derived from a patient's own readily available non-liver cells.

**Statement of Benefit to California:** Like in most states in the US, the number of Californians in need of a liver transplant significantly exceeds the number of available donor organs. Most of these patients have liver cirrhosis due to hepatitis C infection, alcoholic liver disease or cholestatic diseases. Other indications for liver transplantation include acute liver failure, hepatitis B virus infection, metabolic liver diseases and cancer. While the incidence of these liver diseases has been relatively stable, non-alcoholic steatohepatitis (NASH), which was first described only 10 years ago, is rapidly emerging and predicted to become the leading indication for liver transplantation in the future. Because Hispanics have an increased risk of developing NASH, California, the state with the largest Hispanic population in the US, will be particularly impacted by this epidemic. Thus, developing an abundant source of cells for liver cell therapy, as proposed in this project, will not only benefit the Californians currently awaiting liver transplantation, but may also help the state's medical system to respond to this future challenge.